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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/530,094	01/26/2006	Audun Tornes	PN0275	7464

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EXAMINER	
SAMALA, JAGADISHWAR RAO	
ART UNIT	PAPER NUMBER
1618	
MAIL DATE	DELIVERY MODE
07/29/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/530,094	TORNES ET AL.	
	Examiner	Art Unit	
	JAGADISHWAR R. SAMALA	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 June 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-7* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *04/01/2005 & 01/13/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election without traverse of Group I, Claims 1-7 in the reply filed on 06/24/2010 is acknowledged.

- Claims 1-7 are presented for examination and claims 8-14 are withdrawn from consideration.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 04/01/2005 and 01/13/2010 was noted and the submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim recites "at least 50% at a pressure …" It is not clear what is meant by at least 50% at a pressure… assist for detecting the sentinel lymph node. The specification fails to adequately describe "at least 50% at a pressure …" to meet the functional required limitation thereby and to show that the Applicant envisioned what these conditions were at the time of filing.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 4 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Mattrey (WO-00/45855).

Claims are drawn to method for identification of a sentinel lymph node in a subject comprising: administering microbubbles comprising a shell and a gas or gas precursor, said microbubbles having a mean particle size of about 0.25-15 μm in diameter and a pressure stability of at least 50% at a pressure of 120 mm Hg.

Mattrey teaches a method for identifying the sentinel lymph node in a subject preadministered with an ultrasound contrast agents (particularly microbubbles preparations having mean bubble size 1 – 10 μm, that have sufficient pressure 1-2 atm) that are preferentially taken up by the lymphatic system and allow for enhanced visualization of the afferent lymphatics and regional lymph nodes (abstract and page 6 lines 20-30 and page 17 lines 15-20). The microbubble, the shell is formulated from lipids (phospholipids), natural and synthetic polymeric materials (page 15 lines 5-10). Additional disclosure includes that to provide accumulation of a contrast agent in a lymph site, molecules possessing a high affinity to target tissue are preferably used as target agents such as antibodies or their fragments, and receptor ligands reads on macrophage stimulating compounds (page 20 lines 15-19).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mattrey (WO-00/45855) in view of Dugstad et al (US 6,221,337).

Claims are drawn to method for identification of a sentinel lymph node in a subject comprising: administering microbubbles comprising a shell and a gas or gas precursor, said microbubbles having a mean particle size of about 0.25-15 μm in diameter and a pressure stability of at least 50% at a pressure of 120 mm Hg, wherein shell comprises negatively charged phopholipids in an amount of from 50% to 100%.

Mattrey teaches a method for identifying the sentinel lymph node in a subject preadministered with an ultrasound contrast agents (particularly microbubbles preparations having mean bubble size 1 – 10 μm, that have sufficient pressure 1-2 atm)

that are preferentially taken up by the lymphatic system and allow for enhanced visualization of the afferent lymphatics and regional lymph nodes (abstract and page 6 lines 20-30 and page 17 lines 15-20). The microbubble, the shell is formulated from lipids (phospholipids), natural and synthetic polymeric materials. Since the microbubble, preparations includes same phospholipids and incorporating an insoluble gas such as fluorocarbon, that provides for relatively long half-lives and having bubble having mean size in the range of 1-10 microns as recited in claim, would obviously have a pressure stability of at least 50% at a pressure of 120 mm Hg effective in providing enhanced images of lymphatic structures (page 15 lines 5-10). Additional disclosure includes that to provide accumulation of a contrast agent in a lymph site, molecules possessing a high affinity to target tissue are preferably used as target agents such as antibodies or their fragments, and receptor ligands reads on macrophage stimulating compounds (page 20 lines 15-19).

Mattrey fails to teach the shell comprising negatively charged phospholipids.

Dugstad teaches a contrast agent for use in diagnostic studies comprising a suspension in an injectable aqueous carrier liquid of gas microbubbles stabilized by phospholipids-containing amphiphilic material (abstract). Desirably at least 75% of the phospholipid material in the contrast agent consists essentially of phospholipid molecules bearing a net overall charge under, which charge may be positive or, more preferably negative (col. 4 lines 17-22). Additional disclosure includes that the use of charged phospholipids may enable the provision of microbubble contrast agent with advantageous properties regarding, for example, stability, dispersibility and resistance

to coalescence without recourse to additives such as further surfactants and/or viscosity enhancers, thereby ensuring that the number of components administered to the body of a subject upon injection of the contrasts agents is kept to a minimum.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate microbubble stablilzed with negatively charged phosphilipids into Mattrey composition. The person of ordinary skill in the art would have been motivated to make those modifications because Dugstad teaches that use of charged phospholipids may enable the provision of microbubble contrast agent with advantageous properties regarding, for example, stability, dispersibility and resistance to coalescence without recourse to additives such as further surfactants and/or viscosity enhancers, thereby ensuring that the number of components administered to the body of a subject upon injection of the contrasts agents is kept to a minimum (Col 3 lines 65+ and Col. 4 lines 1-8). Therefore, person of ordinary skill in the art would have had a reasonable expectation of success because both Mattrey and Dugstad teaches contrast agents that may used in same field of endeavor such as in a variety of diagnostic imaging techniques including scintigraphy, light imaging, ultrasound for example fundamental and harmonic B-mode imaging and fundamental and harmonic Doppler imaging; if desired three-dimensional imaging techniques.

Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JAGADISHWAR R. SAMALA whose telephone number is (571)272-9927. The examiner can normally be reached on 8.30 A.M to 5.00 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571)272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/J. R. S./
Examiner, Art Unit 1618

/Jake M. Vu/
Primary Examiner, Art Unit 1618